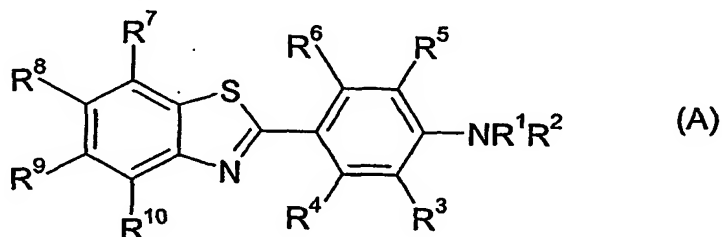


Claims

1. A process for the production of an  $^{18}\text{F}$ -labelled tracer which comprises treatment of a solid support-bound precursor of formula (I)

5 SOLID SUPPORT-LINKER- X -TRACER (I)

wherein X is a group which promotes nucleophilic substitution at a specific site on the attached TRACER and the TRACER is of formula (A)



10

wherein:

$\text{R}^1$  and  $\text{R}^2$  are independently selected from hydrogen, a protecting group,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  hydroxyalkyl, and  $\text{C}_{1-6}$  haloalkyl;

$\text{R}^3$  to  $\text{R}^{10}$  are independently selected from hydrogen, halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  haloalkyl,

15  $\text{C}_{1-6}$  hydroxyalkyl,  $\text{C}_{1-6}$  alkoxy,  $\text{C}_{1-6}$  haloalkoxy, hydroxy, cyano, and nitro;

and one of the groups  $\text{R}^1$  to  $\text{R}^{10}$  is bonded to the SOLID SUPPORT-LINKER-X -;

with  $^{18}\text{F}^-$  to produce the labelled tracer of formula (II)

20  $^{18}\text{F}$ -TRACER (II)

wherein the TRACER is as defined for the compound of formula (I) except that one of the groups  $\text{R}^1$  to  $\text{R}^{10}$  is bonded to the  $^{18}\text{F}$  instead of to the SOLID SUPPORT-LINKER-X - in formula (I);

optionally followed by:

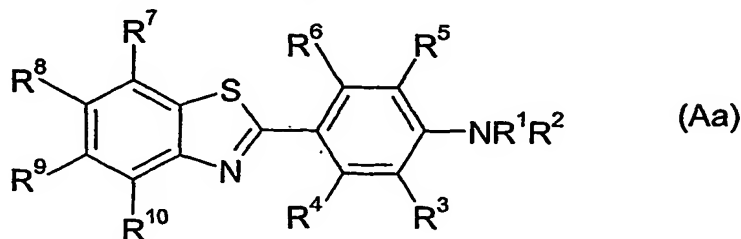
- 25 (i) removal of excess  $^{18}\text{F}^-$ , for example by ion-exchange chromatography; and/or  
 (ii) removal of any protecting groups; and/or  
 (iii) removal of organic solvent; and/or  
 (iv) formulation of the resultant compound of formula (II) as an aqueous solution

2. A process according to claim 1 which comprises treatment of a solid support-bound precursor of formula (Ia):

SOLID SUPPORT-LINKER-SO<sub>2</sub>-O -TRACER (Ia)

5

wherein the TRACER is of formula (Aa)



wherein:

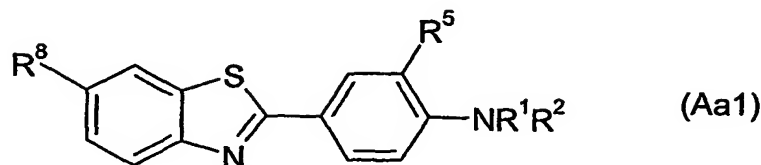
- 10 R<sup>1</sup> and R<sup>2</sup> are independently selected from hydrogen, a protecting group, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> hydroxyalkyl, and C<sub>1-6</sub> haloalkyl;  
 R<sup>3</sup> to R<sup>10</sup> are independently selected from hydrogen, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> hydroxyalkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkoxy, hydroxy, cyano, and nitro;  
in which either (a) an R<sup>1</sup> C<sub>1-6</sub> alkyl group or (b) an R<sup>3</sup> to R<sup>10</sup> C<sub>1-6</sub> alkyl or C<sub>1-6</sub> alkoxy  
 15 group is bonded to the SOLID SUPPORT-LINKER-SO<sub>2</sub>-O – in formula (Ia);

with <sup>18</sup>F<sup>-</sup> to produce the labelled tracer of formula (IIa)

<sup>18</sup>F-TRACER (IIa)

- 20 wherein the TRACER is as defined for the compound of formula (Ia) except that either (a) an R<sup>1</sup> C<sub>1-6</sub> alkyl group or (b) an R<sup>3</sup> to R<sup>10</sup> C<sub>1-6</sub> alkyl or C<sub>1-6</sub> alkoxy group is bonded to the <sup>18</sup>F instead of to the SOLID SUPPORT-LINKER-SO<sub>2</sub>-O – in formula (Ia);  
 optionally followed by:  
 25 (i) removal of excess <sup>18</sup>F<sup>-</sup>, for example by ion-exchange chromatography; and/or  
 (ii) removal of any protecting groups; and/or  
 (iii) removal of organic solvent; and/or  
 (iv) formulation of the resultant compound of formula (IIa) as an aqueous solution.

3. A process according to claim 2 wherein the TRACER is of formula (Aa1)



5 wherein

$R^1$  and  $R^2$  are independently selected from hydrogen, a protecting group,  $C_{1-6}$  alkyl,  $C_{1-6}$  hydroxyalkyl, and  $C_{1-6}$  haloalkyl;

$R^5$  is hydrogen or  $C_{1-6}$  alkyl,

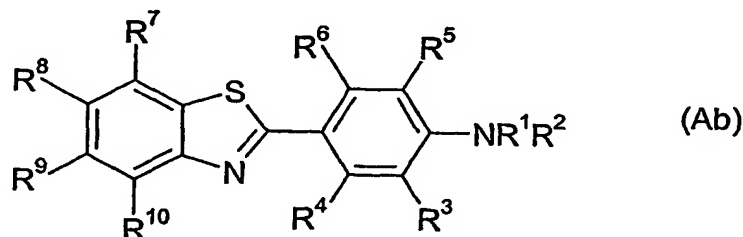
10  $R^8$  is hydroxy,  $C_{1-6}$  alkoxy,  $C_{1-6}$  haloalkyl, or  $C_{1-6}$  alkyl;

provided that one of  $R^1$ ,  $R^5$  and  $R^8$  is  $C_{1-6}$  alkyl bonded to the SOLID SUPPORT-LINKER-SO<sub>2</sub>-O – in formula (Ia) or  $R^8$  is  $C_{1-6}$  alkoxy bonded to the SOLID SUPPORT-LINKER-SO<sub>2</sub>-O – in formula (Ia) .

15 4. A process according to claim 1 which comprises treatment of a solid support-bound precursor of formula (Ib)



wherein  $Y^-$  is an anion and the TRACER is of formula (Ab)



20 wherein:

$R^1$  and  $R^2$  are independently selected from hydrogen, a protecting group,  $C_{1-6}$  alkyl,  $C_{1-6}$  hydroxyalkyl, and  $C_{1-6}$  haloalkyl;

25 one of  $R^3$  to  $R^{10}$  is a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup>- group in formula (Ib) and the others are independently selected from hydrogen, halo,  $C_{1-6}$  alkyl,  $C_{1-6}$

haloalkyl, C<sub>1-6</sub> hydroxyalkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkoxy, hydroxy, cyano, and nitro;

with <sup>18</sup>F<sup>-</sup> to produce the labelled tracer of formula (IIb)

5

<sup>18</sup>F-TRACER (IIb)

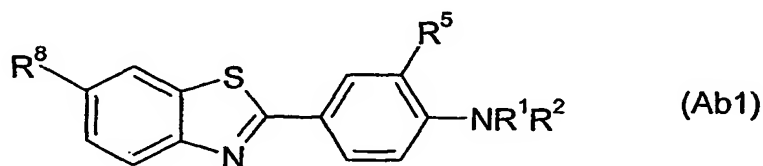
wherein the TRACER is as defined for the compound of formula (Ib) except that one of R<sup>3</sup> to R<sup>10</sup> is a bond to the <sup>18</sup>F instead of a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup>- group in formula (Ib);

10 optionally followed by:

- (i) removal of excess <sup>18</sup>F<sup>-</sup>, for example by ion-exchange chromatography; and/or
- (ii) removal of any protecting groups; and/or
- (iii) removal of organic solvent; and/or
- (iv) formulation of the resultant compound of formula (IIb) as an aqueous solution.

15

5. A process according to claim 4 wherein the TRACER is a compound of formula (Ab1)



wherein:

20

R<sup>1</sup> and R<sup>2</sup> are independently selected from hydrogen, a protecting group, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> hydroxyalkyl, and C<sub>1-6</sub> haloalkyl;

R<sup>5</sup> is hydrogen, C<sub>1-6</sub> alkyl, or a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup>- group in formula (Ib);

25

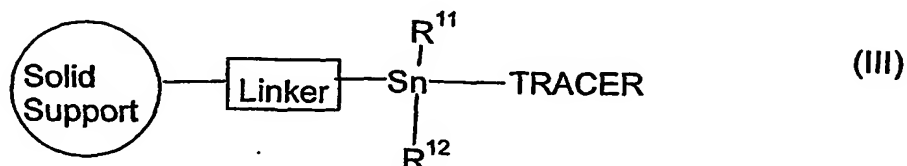
R<sup>8</sup> is hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> alkyl, or a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup>- group in formula (Ib);

provided that only one of R<sup>5</sup> and R<sup>8</sup> is a bond to the SOLID SUPPORT-LINKER-I<sup>+</sup>- group in formula (Ib).

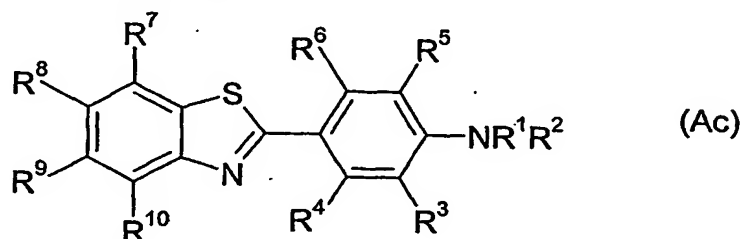
30

6. A process for the production of an <sup>18</sup>F-labelled tracer which comprises

treatment of a solid support-bound precursor of formula (III):



wherein  $R^{11}$  and  $R^{12}$  are independently selected from  $C_{1-6}$  alkyl and the TRACER  
 5 is a compound of formula (Ac):



wherein:

$R^1$  and  $R^2$  are independently selected from hydrogen, a protecting group,  
 10  $C_{1-6}$  alkyl,  $C_{1-6}$  hydroxyalkyl, and  $C_{1-6}$  haloalkyl;

one of  $R^3$  to  $R^{10}$  is a bond to the Sn in formula (III) and the others are  
 independently selected from hydrogen, halo,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$   
 hydroxyalkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  haloalkoxy, hydroxy, cyano, and nitro;

15 with a source of  $^{18}\text{F}$ , suitably  $^{18}\text{F}_2$ ,  $^{18}\text{F}-\text{CH}_3\text{COOF}$  or  $^{18}\text{F}-\text{OF}_2$ ;

to give the labelled tracer of formula (IV);

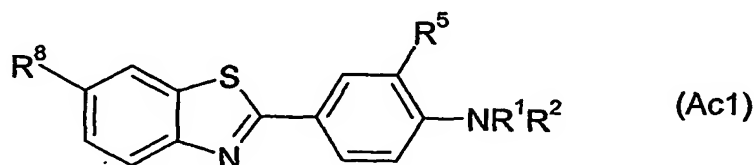
20  $^{18}\text{F}$ -TRACER (IV)

wherein the TRACER is as defined for the compound of formula (III) except that  
 one of  $R^3$  to  $R^{10}$  is a bond to the  $^{18}\text{F}$  instead of a bond to the Sn in formula (III);  
 optionally followed by:

(i) removal of excess fluorinating agent and  $^{18}\text{F}^-$  ions produced in the generation  
 25 of the fluorinating agent or in the reaction; and/or  
 (ii) removal of any protecting groups; and/or

- (iii) removal of organic solvent; and/or
- (iv) formulation of the resultant compound of formula (IV) as an aqueous solution.

7. A process according to claim 6 in which the TRACER is suitably a compound of  
 5 formula (Ac1)



wherein:

- $R^1$  and  $R^2$  are independently selected from hydrogen, a protecting group,  $C_{1-6}$  alkyl,  $C_{1-6}$  hydroxyalkyl, and  $C_{1-6}$  haloalkyl;
- $R^5$  is hydrogen,  $C_{1-6}$  alkyl, or a bond to the Sn in formula (III);
- $R^8$  is hydroxy,  $C_{1-6}$  alkoxy,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  alkyl, or a bond to the Sn in formula (III);
- provided that only one of  $R^5$  and  $R^8$  is a bond to the Sn in formula (III).

15

8. A process for the preparation of a  $^{18}\text{F}$ -labelled tracer of formula (II), (IIa), (IIb), or (IV), according to any one of claims 1 to 7, for use in PET.

20

9. A compound of formula (I), (Ia), (Ib), (III) as defined in any one of claims 1 to 7.

10. A radiopharmaceutical kit for the preparation of an  $^{18}\text{F}$ -labelled tracer for use in PET, which comprises:

(i) a vessel containing a compound of formula (I), (Ia), or (Ib) as defined in any one of claims 1 to 5; and

25 (ii) means for eluting the vessel with a source of  $^{18}\text{F}^-$  ;

(iii) an ion-exchange cartridge for removal of excess  $^{18}\text{F}^-$ ; and optionally

(iv) a cartridge for solid-phase deprotection of the resultant product of formula (II), (IIa), or (IIb) as defined in any one of claims 1 to 5.

30 11. A cartridge for a radiopharmaceutical kit for the preparation of an  $^{18}\text{F}$ -labelled

tracer for use in PET which comprises:

- (i) a vessel containing a compound of formula (I), (Ia), or (Ib) as defined in any one of claims 1 to 5; and
- (ii) means for eluting the vessel with a source of  $^{18}\text{F}^-$ .

5

12. A radiopharmaceutical kit for the preparation of of an  $^{18}\text{F}$ -labelled tracer for use in PET, which comprises:

- (i) a vessel containing a compound of formula (III) as defined in claim 6 or 7; and
- 10 (ii) means for eluting the vessel with a source of  $^{18}\text{F}$ ; and optionally
- (iii) a cartridge for removal of excess fluorinating agent and  $^{18}\text{F}^-$  ions; and optionally
- (iv) a cartridge for solid-phase deprotection of the resultant product of formula (IV) as defined in claim 6 or 7.

15

13. A cartridge for a radiopharmaceutical kit for the preparation of an  $^{18}\text{F}$ -labelled tracer according to claim 12 for use in PET which comprises:

- (i) a vessel containing a compound of formula (III) as defined in claim 6 or 7; and
- (ii) means for eluting the vessel with a source of  $^{18}\text{F}$ .

20

14. A method for obtaining a diagnostic PET image which comprises the step of using a radiopharmaceutical kit according to claim 10 or 12 or a cartridge for a radiopharmaceutical kit according to claim 11 or 13.